

In the Claims:

1. (Currently Amended) A method of identifying at least one chemical compounds that interact with an enzyme ~~a target molecule~~ comprising the steps of:
 - a) mixing a substrate or product of said enzyme ~~a target~~ with at least one said chemical compounds;
 - b) generating a first NMR spectrum that displays either a chemical shift in the first dimension or a chemical shifts in the other dimension of said substrate or product in step a);
 - c) exposing the mixture of said substrate or product and ~~mixture of~~ at least one said chemical compounds in step a) to said enzyme ~~a target molecule~~ for one or more incubation times;
 - d) generating a second NMR spectrum that displays either a chemical shift in the first dimension or a chemical shifts in the other dimension of substrate or product in step a) that has been exposed to said enzyme ~~the target molecule~~ in step c) in the presence of at least one ~~one or mixture of~~ chemical compounds in step a);
 - e) comparing said first NMR spectrum and second NMR spectrum after one or more said incubation times in step c) to determine at least one difference between said first NMR spectrum and second NMR spectrum, the differences observed along either or both chemical shift dimensions identifying ~~the transformation of~~ said substrate or product and classifying the presence of at least one ~~said one or more~~ chemical compounds that interact with said enzyme ~~target molecule~~.
2. (Cancelled)
3. (Currently Amended) The method of claim 1 wherein at least one said chemical compound of step a) ~~further comprises a chemical compound that~~ is in solution or attached to a solid substrate or matrix.
4. (Currently Amended) The method of claim 1 wherein said first NMR spectrum of step b) is selected from ~~further comprises a first spectrum selected from~~ the group consisting of a one-dimensional, two-dimensional and three-dimensional spectrum.
5. (Currently Amended) The method of claim 4 wherein said first NMR spectrum displays a chemical shift in said first dimension selected from the group consisting of 1H, 3H, 11B, 13C, 15N, 19F, 29S and 31P ~~1H, 3H, 11B, 13C, 15N, 19F, 29S or 31P~~ chemical shift, and a chemical shift in said other dimension selected from the group consisting of 1H, 3H, 11B, 13C, 15N, 19F, 29S and 31P ~~1H, 3H, 11B, 13C, 15N, 19F, 29S or 31P~~ chemical shift.
6. (Currently Amended) The method of claim 1 wherein said mixture of exposing step of step c) ~~further comprises a mixture comprising~~ between 2 and 100 chemical compounds.

7. (Original) The method of claim 1 wherein said incubation times number between 1 and 20, 30, 40, 50 or greater.

8. (Currently Amended) The method of claim 1 wherein step d) said second spectrum displays a chemical shift in said first NMR dimension selected from the group consisting of 1H, 3H, 11B, 13C, 15N, 19F, 29S and 31P ~~1H, 3H, 11B, 13C, 15N, 19F, 29S or 31P~~ chemical shift, and a chemical shift in said other dimension selected from the group consisting of 1H, 3H, 11B, 13C, 15N, 19F, 29S and 31P ~~1H, 3H, 11B, 13C, 15N, 19F, 29S or 31P~~ chemical shift.

9. (Cancelled)

10. (Original) The method of claim 1 wherein the determining step of step e) comprises a method selected from the group consisting of an algorithm, a computer algorithm, and visual inspection.

11. (Cancelled).

12. (Withdrawn) A method of determining an interaction constant (α) comprising the steps of: a) exposing a substrate or product to a target molecule for one or more incubation times; b) generating a first spectrum that displays either a chemical shift in the first dimension or a chemical shifts in an other dimension of the substrate or product in step a) that has been exposed to the target molecule; c) mixing a substrate with the first ligand; d) exposing the substrate and the first ligand to the target molecule for one or more incubation times; e) generating a second spectrum that displays either a chemical shift in the first dimension or a chemical shift in the other dimension of substrate or product in step c) that has been exposed to the target molecule in step d) in the presence of the first ligand in step c); f) mixing the substrate or product with one or more chemical compounds; g) exposing the substrate or product and one or more chemical compounds to a target molecule for one or more incubation times; h) generating a third spectrum that displays either a chemical shift in the first dimension or a chemical shift in the other dimension of substrate or product in step f) that has been exposed to the target molecule in step g) in the presence of the one or more chemical compounds in step f); i) mixing substrate or product with first ligand and one or more chemical compounds; j) exposing the substrate or product, the first ligand and the one or more chemical compounds to the target molecule for one or more incubation times; k) generating a fourth spectrum that displays either a chemical shift in the first dimension or a chemical shift in the other dimension of the substrate or product in step i) that has been exposed to the target molecule in step j) in the presence of the first ligand and the one or more chemical compounds in step f); l) determining a conversion rate or conversion rates of each substrate or product from each spectrum of steps b), e), h) and k); and deriving an interaction constant (α) from a steady-state rate equation.

13. (Withdrawn) A method using NMR for of screening for ligands which exhibit synergistic effects on a target in the presence of another ligand.

14. (Withdrawn) The method of claim 12 wherein the target is an enzyme comprising more than two binding sites.

15. (Withdrawn) The method of claim 14 wherein the two binding sites are a substrate- and co-enzyme-binding site.

16. (Withdrawn) The method of claim 12 wherein the rate is determined by the following equation:

$$v = V_m / \left[1 + \left(\frac{K_M}{S} \right) \left(1 + \frac{I_1}{K_{EI1}} + \frac{I_2}{K_{EI2}} + \frac{I_1 I_2}{\alpha K_{EI1} K_{EI2}} \right) \right]$$

wherein S, I₁ and I₂ are the substrate, inhibitor I₁ and inhibitor I₂ concentrations, respectively.

17. (Previously Presented) The method of claim 1 wherein said at least one chemical compound is provided in a multiwell vessel loaded with target and substrate-or product.

18. (Original) The method of claim 17 wherein a target-substrate reaction is quenched at a selected time.

19. (Currently Amended) A method of identifying compounds that interact with an enzyme ~~a target molecule~~ comprising the steps of:

- a) exposing substrate to said enzyme ~~a target molecule~~ for one or more incubation times;
- b) generating one or more NMR spectra at one or more incubation times of said substrate and said enzyme ~~target molecule~~ of step a),
- c) exposing said substrate and one or a mixture of chemical compounds for one or more incubation times;
- d) generating one or more NMR spectra at one or more incubation times of said substrate, said enzyme ~~target molecule~~ and said one or a mixture of chemical compounds of step c);
- e) comparing at least one NMR spectrum of step b) with at least one NMR spectrum of step d) to determine at least one difference between said NMR spectrum of step b) with said NMR spectrum of step d), the differences observed along either or both chemical shift dimensions identifying ~~the~~ transformation of said substrate and classifying the presence of one or more compounds that interact with said enzyme ~~target molecule~~.